REMARKS

Entry of the foregoing, reexamination and reconsideration of the subject application, as amended, pursuant to and consistent with 37 C.F.R. §1.112, are respectfully requested in light of the remarks which follow.

I. Amendments to the Claims

By the foregoing amendments to the claims, claims 23, 24, 26-29, 33, 35 and 41 have been amended, and new claim 43 has been added.

In particular, claim 23 has been amended by canceling the phrases "and/or prevention" and "or characterized by."

Additional amendments to the claims have also been made to clarify the claim language, for consistency, and to bring the claims into better conformance with U.S. patent practice. These amendments are merely editorial in nature and are not intended to change the scope of the claims or any elements recited therein.

The amendments to the claims, including cancellation of claims, have been made without prejudice or disclaimer to any subject matter recited or canceled herein. Applicants reserve the right to file one or more continuation and/or divisional applications directed to any canceled subject matter. No new matter has been added, and entry of the foregoing amendments to the above-identified application are respectfully requested.

III. Response to Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

At pages 6-7 of the Office Action, claims 23-35 and 41-42 have been rejected under 35 U.S.C. § 112, second paragraph, as purportedly being indefinite for the following reasons.

A. The Examiner has stated that claim 23 is indefinite because it is not clear how SEQ ID NOS: 3-6 can define the sequence of Formula I.

In response, Applicants have amended claim 23 by deleting the parenthetical phrase "(Formula I; SEQ ID NOS: 3-6)." SEQ ID NOS: 3-6 are recited in new dependent claim 43.

B. The Examiner has stated that claim 23 is indefinite because it is not clear what the "I" in "Formula I" stands for.

Claim 23 has been amended to recite the full names of the amino acids, rather than their corresponding one-letter codes. Thus, it is clear that the "I" refers to Roman numeral "I" and does not refer to isoleucine.

C. The Examiner has stated that claim 23 is indefinite because the difference between a "condition *associated* with" and a "condition *characterized* by" pathological loss of nervous tissue is not clear.

Applicants submit that a person of ordinary skill in the art would recognize that the phrase "condition associated with a pathological loss of nervous tissue" encompasses conditions identified in the present specification as "characterized by a pathological loss of nervous tissue " as well as other conditions included in the envisioned diseases to be treated with AF, which are typically characterized not by the loss of nervous tissue, but by a series of other markers. Thus, although these other conditions are clearly associated with loss of nervous tissue, a medical doctor would most likely diagnose them due to their more easily accessible characteristics instead of starting out with a brain scan.

However, to expedite prosecution in the present application, and not to acquiesce to the Examiner's rejection, claim 23 has been amended by deleting recitation of "characterized by."

D. The Examiner has stated that claims 23 and 41 are indefinite for reciting "an antisecretory protein" and "antisecretory factors," respectively.

Claims 23 and 41 have been amended to recite "antisecretory factor (AF) protein." As clearly described at page 4, lines 9-16, of the present specification, AF protein is defined as a class of proteins of varying lengths, the full-length protein of which has a length of 382 amino acids. Post-translational processing of the full-length protein in the cell leads to a variety of different peptides and protein fragments of AF with biological activity. This is well-documented knowledge in the field (see, e.g., W097/008202). Thus, a person of ordinary skill in the art would recognize that that the "AF proteins and derivatives thereof" of claim 23 encompass not only full-length AF but also fragments and variants of AF, so long as they comprise the amino sequence of Formula I.

Applicants submit that the claims as amended particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 112, second paragraph, rejections.

III. Response to Claim Rejections Under 35 U.S.C. § 112, First Paragraph

A. At pages 8-16 of the Office Action, claims 23-35 and 41-42 have been rejected under 35 U.S.C. § 112, first paragraph, as purportedly lacking enablement.

Specifically, the Examiner has acknowledged that the specification enables treatment methods of increasing neuronal proliferation by administering the active N-terminal region of ASAP (amino acids 1-163) or a fragment thereof (amino acids 36-51) for conditions associated with a pathological loss of nervous cells or tissue or memory loss. However, the Examiner has also stated that the specification does not enable treatment by administering all of the peptides encompassed by Formula I. According to the Examiner, it is not clear what other peptides of Formula I might possess the desired activity. In addition, the Examiner has stated that the specification does not enable "prevention" of the recited conditions.

B. At pages 16-20 of the Office Action, claims 23-35 and 41-42 have been rejected under 35 U.S.C. § 112, first paragraph, as purportedly failing to comply with the written description requirement.

Similar to above, the Examiner has stated that the description of two polypeptides (amino acids 1-163 and 36-51 of SEQ ID NO: 1) does not adequately describe the genus of functionally equivalent polypeptides encompassed by the present claims.

The rejections under 35 U.S.C. § 112, first paragraph, are respectfully traversed for at least the following reasons.

Applicants respectfully note that the induction of AF by, e.g., SPC, as demonstrated in examples 3 and 4 in the present specification, will not lead to the formation of one full-length AF protein only. On the contrary, as already outlined above, and clearly described in the specification, AF is known and defined as comprising proteins and peptides of varying lengths, brought on by natural post translational processing of the full-length protein (see, e.g., W0971008202).

Applicants further note that AF-16 (SEQ ID NO: 2), which has actually been proven to have the new and surprising desired biological effect, has previously been shown to have a similar biological activity as the full-length protein. In addition, that biological activity is maintained in even shorter fragments of AF, and even by synthetically produced peptides (see, e.g., W0971008202). Although the '202 publication does not teach or suggest that AF could be used to treat or prevent pathological loss or gain of nervous tissue, the reference does teach that AF can be produced recombinantly and that even smaller fragments and synthetic peptides displayed a biological activity similar to the one at that time known for the full-length AF protein.

Furthermore, the present inventors have meanwhile been able to prove still another

biological activity for AF and AF-16, as well as for several other and shorter peptides (see, e.g., WO 2007/126364). Thus, a person of ordinary skill in the art, being made aware of this new medical indication, namely the possibility to rescue neuronal tissue or to stimulate *de novo* production of neuronal stem cells, would of course anticipate that the same peptides and fragments should be usable for the new biological activity as well. Applicants submit that a person of ordinary skill in the art would reasonably predict that all of the sequences encompassed in the present claims would be suitable for the recited methods.

With regard to "prevention," as noted above this term has been deleted from the claims. Accordingly, this aspect of the rejection is moot.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

IV. Response to Claim Rejections Under 35 U.S.C. § 102

At page 20-22 of the Office Action, claims 23-35, 41, and 42 have been rejected under 35 U.S.C. § 102(b) as purportedly being anticipated by St. George-Hyslop et al., WO 97/27296 as evidenced by Barten et al. (Mol Neurobiol., 2008) and Roth et al. (Biol Res., 2005). This rejection is respectfully traversed.

It is well established that for prior art to be anticipatory, every element of the claimed invention must be disclosed in a single item of prior art in the form literally defined in the claim. *See, e.g., Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 213 U.S.P.Q. 81, 90 (Fed. Cir. 1986). Applicants submit that WO 97/27296 fails to satisfy this requirement, for at least the following reasons.

The Examiner has stated that W097127296 discloses the use of the entire S5a protein for treating Alzheimer's disease, or affinitive diseases. Applicants submit, however, that W097/27296 actually teaches that only a portion of S5a is interacting with presenilin and thus may have an effect on Alzheimer's disease. On page 15, lines 8-13 of the reference, it is clearly stated that "two overlapping clones have been identified as representing a portion of the human protein alternatively known as Antisecretory factor (AF) or the Multiubiquitin chain binding S5a subunit of the 26S proteasome." The next sentence further states that "These clones, which together include residues 70-377 of S5a, were shown to interact with the normal presenilin..." Thus, the only disclosed pharmaceutical preparations of W097/27296, which are to be used for treating Alzheimer's disease, are those that

comprise said PS-interacting proteins disclosed in the application, i.e. those which include residues 70-377 of S5a.

In conclusion, actually only the part of S5a comprising residues 70-377 was in W097127296 shown to be able to bind to presenilin, thus, only this part of S5a was shown to be useful for treating Alzheimer's disease. According to W097/27296, it is the ability of S5a to bind presenilin that makes it suitable for treating Alzheimer's disease, an activity which, as outlined above, resides exclusively in residues 70-377 (see page 15, lines 7-page 18, line 24).

Applicants also note that even though the amino acid sequence of S5a is highly similar to the amino acid sequence of AF, some differences still exist. Thus, the proteins are not interchangeable. These differences are all located within the part of S5a which in W097127296 has been shown to be responsible for facilitating the presenilin binding activity.

Applicants further submit that WO97/27296 does not disclose the use of AF proteins and derivatives thereof comprising an amino acid sequence of Formula I, as recited in the present claims. In particular, Formula I does not encompass residues 70-377 of S5a. AF-16, for example is located at residues 36-51, thus clearly outside the amino acid residues which in W097/27296 are described as responsible for the presenilin-binding activity of S5a.

Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSION

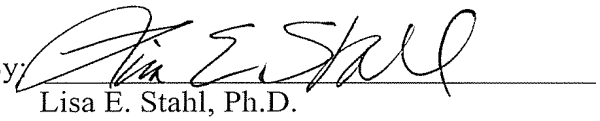
From the foregoing, further and favorable action in the form of a Notice of Allowance is respectfully requested and such action is earnestly solicited.

In the event that there are any questions concerning this amendment or the application in general, the Examiner is respectfully requested to telephone the undersigned so that prosecution of the application may be expedited.

Respectfully submitted,

BUCHANAN INGERSOLL PC

Date: April 23, 2009

By: 

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